

I. REMARKS

Upon entry of the foregoing amendment, claims 1-14 and 17-20 are pending in the present application. Claims 15-16 were previously cancelled. Claims 18-20 stand withdrawn.

Applicants have amended claims 1-3 solely to advance prosecution. Applicants, by amending any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert any of the claims canceled herein or the original claim scope of any claim amended herein, in a continuing application.

It is believed this amendment does not introduce new matter and entry is respectfully requested.

II. REJECTION OF CLAIMS 1-3 UNDER 35 USC § 112

At page 2 of the Official Action, the Examiner has rejected claims 1-3 under 35 USC § 112. The Examiner states that these "claims still have several provisos and it is not clear what is actually claimed."

RESPONSE

Applicants have amended claims 1-3 and have canceled the provisos from these claims. As such, reconsideration and withdrawal of this rejection is respectfully requested.

III. REJECTION OF CLAIMS 1-8, 10-14 AND 17 UNDER 35 USC § 103(a)

At page 3 of the Official Action, the Examiner has maintained the rejection of claims 1-8, 10-14 and 17 under 35 USC § 103(a) as being unpatentable over Zhang et al. (WO 2003/51877) in view of Bauser et al. (WO 03014117) and Bauser et al. (WO 03014116).

RESPONSE

The rejection is respectfully traversed. The Examiner has not established a *prima facie* case of obviousness against the presently pending claims.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, there must be some motivation or teaching in the references cited by the Examiner to combine the separate elements taught in the separate references. As the U.S. Supreme Court held in *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 (2007), “a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed

new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.” See *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 at 417-418. Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

In response to applicants arguments and evidence rebutting the Examiner’s position filed in the last Response and Amendment on October 27, 2009, the Examiner states on page 3, in relevant part, that

“The declaration does not provide any comparative results. It just states their compounds with the limited R5 and R4 to be H are superior is not convincing. Besides the claims still have R51 to be a H and R4 and R5 together form a bond which reads on the prior art. See page 11 of the previous Office Action.”

Applicants take serious issue with these statements.

First, the Declaration filed with the previous Response and Amendment clearly provides comparative data. In particular, the Declaration contains evidence which compares no fewer than twenty separate compounds – ten of which have a hydrogen atom at the position that corresponds to the presently claimed “R5” position and ten of which are identical in every respect except for containing a non-

hydrogen group at the same substituent. The Declaration further provides quantitative information regarding each of these compounds – specifically the “gain in potency of PDE10 inhibition” and “gain in selectivity for PDE10 over PDE4”. Therefore, the Declaration indeed *compares* the effects of having a hydrogen atom as the R5 substituent with the effects of having a non-hydrogen group as the R5 substituent.

Second, applicants take issue with the statement that “[b]esides the claims still have R51 to be a H”. It appears to applicants that the Examiner is implying that because R51 of the presently pending claims may still be a hydrogen moiety, the data provided in the Declaration is somehow invalid for demonstrating the unexpected results. To the contrary, R51 possibly defined as hydrogen is wholly consistent with the comparative data provided in the Declaration. In fact, each of the comparative examples in the first column of Table 1 in the Declaration has R51 as hydrogen, whereas the comparative examples in the second column of Table 1 each have both R5 and R51 as hydrogen. Applicants respectfully point out to the Examiner that the whole point of the data is to demonstrate the difference in compounds that have R5 and R51 both = H vs. R5 as a non-hydrogen moiety.

Third, applicants take issue with the Examiner’s statement that “R4 and R5 together to form a bond which reads on the prior art.” This is simply not true. The presently pending claims recite the possibility that “R4 and R5 together form a 1-4C-alkylene bridge”, however they do not allow for R4 and R5 together to form a bond.

As argued in the previous Response and Amendment, the Zhang et al. and Bauser et al. compounds all have nothing else but hydrogen at the 5-position of the tricyclic scaffold. In particular, in the case of the Zhang et al. compounds, R5 = R51 = H and in the case of the Bauser compounds, R5 = H and R51 is missing due to the ring double bond. In contrast, the presently amended claims may only have "1-4C-alkyl, cyano or 1-4C-alkoxycarbonyl" at the R5-position of the tricyclic scaffold, while R51 may be H or 1-4C alkyl. Applicants have canceled the possibility of R5=H from the presently pending claims.

Further, applicants have already submitted a Declaration under 37 CFR §1.132 which demonstrates the "superior unexpected results" as requested by the Examiner in the previous Official Action. In the Declaration, similar compounds were tested wherein R5 = H was substituted for a compound that falls within the scope of currently pending claim 1.

The Declaration clearly demonstrates that the compounds as claimed in presently pending claim 1 show a totally unexpected biological profile which by no means was suggested or implied by the compounds known from the art. In particular they show a superior pharmacological profile as PDE10 inhibiting compounds, since they unexpectedly show an increased potency regarding PDE10 inhibition and/or an increased selectivity for PDE10 over PDE4 when compared to compounds from the art where R5 is hydrogen.

These findings are completely unexpected in view of the teachings of the prior art which merely show that compounds of formula 1 with R5 being hydrogen are capable of inhibiting PDE10. As such, a person of ordinary skill in the art would not expect that replacing hydrogen in the R5 position by alkyl, alkoxycarbonyl, or cyano would lead to compounds with increased potency regarding PDE10 inhibition and/or an increased selectivity for PDE10 over PDE4.

As such, the presently rejected claims are unobvious over the cited references and withdrawal of this rejection is respectfully requested.

IV. PROVISIONAL REJECTION OF CLAIMS 1 AND 17 UNDER THE DOCTRINE OF OBVIOUSNESS-TYPE DOUBLE PATENTING

At page 3 of the Official Action, the Examiner states that she has maintained the provisional rejection of claims 1 and 17 under the doctrine of obviousness-type double patenting over USSN 10/562,149.

RESPONSE

The provisional rejection is respectfully traversed. The presently pending application and the '149 application are no longer commonly owned. Therefore, the Examiner cannot reject the presently pending claims using the '149 application as a reference.

Reconsideration and withdrawal of this provisional rejection is respectfully requested.

**V. PROVISIONAL REJECTION OF CLAIMS 1-14 AND 17 UNDER THE DOCTRINE OF
OBVIOUSNESS-TYPE DOUBLE PATENTING**

At page 3 of the Official Action, the Examiner states that she has maintained the provisional rejection of claims 1-14 and 17 under the doctrine of obviousness-type double patenting over USSN 11/794,494.

RESPONSE

This provisional rejection is respectfully traversed. The presently pending application and the '494 application are no longer commonly owned. Therefore, the Examiner cannot reject the presently pending claims using the '494 application as a reference.

Reconsideration and withdrawal of this provisional rejection is respectfully requested.

**VI. PROVISIONAL REJECTION OF CLAIMS 1-14 AND 17 UNDER THE DOCTRINE OF
OBVIOUSNESS-TYPE DOUBLE PATENTING**

At page 3 of the Official Action, the Examiner states that she has maintained the provisional rejection of claims 1-14 and 17 under the doctrine of obviousness-type double patenting over USSN 11/794,497.

RESPONSE

This provisional rejection is respectfully traversed. All current rejections have been overcome with the amendments and remarks made herein. Therefore, the Examiner must withdraw this provisional rejection because the '497 application was filed later than the presently pending application.

Reconsideration and withdrawal of this provisional rejection is respectfully requested.

VII. REJECTION OF CLAIMS 1-9 UNDER 35 USC § 103(a)

At page 4 of the Official Action, the Examiner has newly rejected claims 1-9 under 35 USC § 103(a) as being unpatentable over Caplus English Abstract DN 125:247578, 1996.

RESPONSE

The rejection is respectfully traversed. The Examiner has not established a *prima facie* case of obviousness against the presently pending claims.

The requirements for establishing a *prima facie* case of obviousness are outlined in section III above.

The Examiner has stated on pages 5-6 the following, in relevant part:

The difference [between the prior art and the presently pending claims] is in R5 and R51 position. In applicants amended claims R5 is not H. However, R51 can be a H.

The previous 103 rejection had a similar reasoning. Applicants filed a declaration with a statement saying that their compounds are superior without any side by side comparison. The deficiency between the

prior art and the applicants compound is a H v methyl, and that modification is prima-facie obvious in the absence of unexpected results.

Again, applicants take issue with several of the Examiner's statements. First, as outlined above in section III, the Declaration filed with the previous Response and Amendment did indeed provide comparative data (i.e. a "side by side comparison"). Specifically, the Declaration compared compounds in the prior art that had R5 = H vs. compounds according to the present claims that have R5 = 1-4C alkyl, cyano or 1-4C-alkoxycarbonyl. Therefore, the "unexpected results" that the Examiner is requesting can clearly be found in the as-filed Declaration.

Second, applicants respectfully submit that the only difference between the cited art and the presently pending claims is not at the R5 position as alleged by the Examiner. In particular, in the position that corresponds to the R6 substituent, the prior art requires a carbonyl moiety. However, the presently claimed R6 substituent is "1-6C alkyl or 1-4C alkyl substituted by R61". The prior art cited by the Examiner does not teach such a substituent according to the presently pending claims. Therefore, the Caplus reference cited by the Examiner does not teach or suggest all the limitations of the claims as required by *In re Wilson*.

Reconsideration and withdrawal of this rejection is respectfully requested.

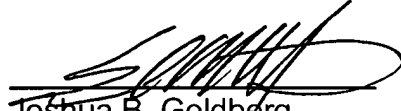
VIII. CONCLUSION

Applicants assert that the claims are in condition for immediate allowance and early notice to that effect is earnestly solicited. Should the Examiner deem that any further action by Applicants' undersigned representative is desirable and/or necessary, the Examiner is invited to telephone the undersigned at the number set forth below.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

THE NATH LAW GROUP



Joshua B. Goldberg
Registration No. 44,126
Sheldon M. McGee
Registration No. 50,454
Customer No. 34375

Date: June 15, 2010
THE NATH LAW GROUP
112 South West Street
Alexandria, Virginia 22314
Tel: (703) 548-6284
Fax: (703) 683-8396
JBG/SMM/ROA.doc